

High-resolution computed tomography features of idiopathic pulmonary alveolar proteinosis

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Aims and objectives

Pulmonary alveolar proteinosis (PAP) is a rare disease characterized by alveolar deposition of surfactant-like or periodic acid-schiff proteins [1,2]. Since the first description of PAP by Rosen et al. [3], this disease has been reported mainly in the case reports or some limited studies [4]. PAP has three forms: congenital, idiopathic (primary), and secondary. Idiopathic form is the most common type accounting for about 90% of all PAPs [1]. Secondary PAP usually occurs due to exposure to some materials such as silica, cement, aluminum, titanium or nitrogen dioxide. It may also be secondary to a hematologic malignancy or various types of immunodeficiency disorders [1,2,5]. Indeed, PAP is the final outcome of surfactant and pulmonary immune disorders and elevated serum granulocyte-monocyte colony stimulating factor (GM-CSF) antibodies are seen in idiopathic PAP [6,7,8]. It is postulated that these antibodies prevent the final differentiation of alveolar macrophages and thereby interfere with surfactant clearance [1,8]. Typical radiographic appearance of PAP is bilateral symmetric opacities with sparing of apices and costophrenic angles [1]. Less frequently it may appear as multifocal asymmetric opacities or consolidations [1,2]. In some cases, especially in moderate disease, the radiographic involvement may be greater than clinical presentation (clinico-radiologic discrepancy)[9]. Computed tomography, especially high resolution computed tomography (HRCT), demonstrates more details of lung involvement. Crazy-paving pattern (network-like thickened septal lines on a background of ground-glass opacity) was first reported for PAP [10]. This pattern in PAP usually is bilateral and extensive with intervening intact geographic or lobular areas¹. Crazy-paving has no specific zonal distribution [11,12,13]. Although crazy-paving is characteristic for PAP, some other diseases may result in similar pattern, including pulmonary hemorrhage, infections, pulmonary edema, inhalation disorders, malignancies (bronchioalveolar carcinoma, lymphangitic carcinomatosis), radiation, and some drugs [1,14,15,16]. Because the crazy-paving pattern is not specific for PAP and related studies on this issue are lacking and also other diseases can mimic this pattern, new studies may help us to better understand the more specific radiologic presentations of idiopathic PAP. Furthermore, familiarity with various pattern of lung involvement on HRCT of patients with idiopathic PAP is essential for early diagnosis of this life threatening disorder and decreasing its morbidity and mortality.

Methods and materials

Thirty five consecutive patients (mean age 38 ± 14 (range: 4-68) years; 54.3% male) with proven PAP (by lung biopsy [n=10] or bronchoalveolar lavage[n=25]) from Mar. 2006 to Mar. 2011 in Masih Daneshvary hospital of Tehran (a tertiary center for lung diseases) entered to the study. All patients had idiopathic PAP without any underlying diseases.

All chest HRCT images (SIEMENS SOMATOM EMOTION, Germany) were reviewed by two expert pulmonary radiologists with 17 and 10 years of experience with high interobserver agreement ($\kappa=0.85$).

Results

All patients had diffuse bilateral lung involvement that was symmetric in 97%. One patient had bilateral multifocal asymmetric lung involvement. Interlobular septal thickening (ILST) was the most common HRCT finding which was seen in all patients. The second most common HRCT feature was ground glass opacities (GGOs) (91.7%). Crazy-paving pattern was seen in 29 (83%) patients. Indeed, the main HRCT presentation of PAP was crazy-paving which is a combination of septal thickening and GGOs. ILST and GGO without crazy-paving were seen in 17% and 14.7% of patients, respectively.

The overall extent of parenchymal involvement was 50 to 75% in eighty percent of patients and 25 to 50% in twenty percent. The dominant distribution of disease was diffuse involvement of all lung zones (85.7%). Only 14.3% of patients had randomly spared upper or lower zones.

Thirty three cases (94%) had areas of geographic sparing within the affected lung. Peripheral sparing was seen in 85.7% of patients, including three patterns with some overlap: costophrenic angle (80%), apices (60%), and subpleural (57%) sparing.

The other common HRCT finding of our patients was consolidation which was seen in 22 patients (63%). Other findings included pulmonary nodules (31.4%), mediastinal and/or hilar lymphadenopathy (23%), mass like consolidation (17%), pleural effusion (8.6%) and honey combing (5.7%). All HRCT features of patients with PAP are shown in table 1.

The vast majority of pulmonary HRCT findings were in association with crazy-paving pattern, except for pleural effusion; all three patients with pleural effusion had not crazy-paving.

The HRCT features of six patients without crazy-paving were: ILST (n=6), GGOs (n=5), pulmonary nodules (n=5), consolidations (n=4), hilar or mediastinal lymphadenopathy (n=3), mass like consolidation (n=3), and pleural effusion (n=3).

There was no statistically significant difference in HRCT presentations of PAP between age groups. All female patients (n=16) had crazy-paving, while 13 out of 19 (68%) male patients had crazy-paving on their lung HRCT ($p=0.02$).

Images for this section:

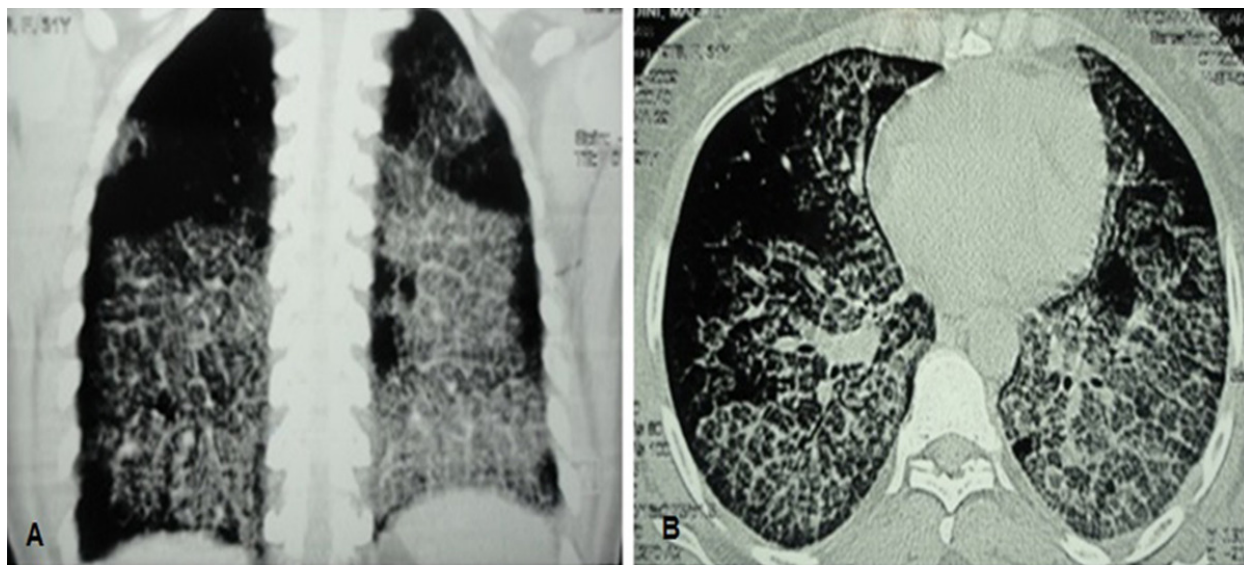


Fig. 1: Coronal reconstructed (A) and axial (B) HRCT images of a 31 year female with idiopathic PAP presenting with dyspnea and cough. Bilateral widespread crazy-paving pattern is seen. Costophrenic, subpleural and apical sparing is well evident in coronal image.



Fig. 2: Axial HRCT images of a 40 year man with idiopathic PAP demonstrat bilateral widespreed crazy-paving pattern and a mass-like consolidation in left lower lobe.

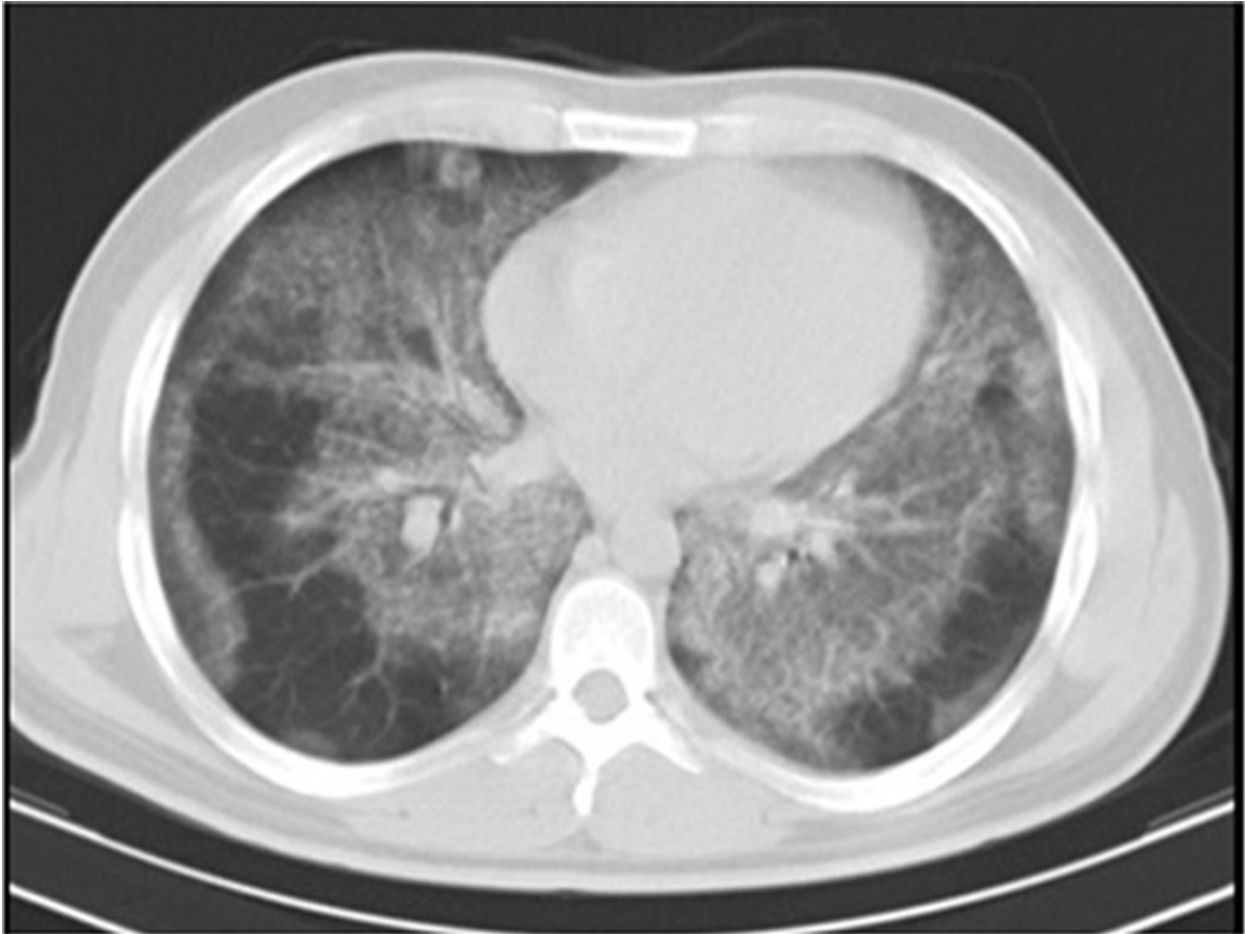


Fig. 3: Bilateral tiny nodular infiltration and ground glass opacities along with subpleural sparing in a 41 year man with idiopathic PAP.

| HRCT findings | | Sex | | Age group | | | Total (n=35) |
|--------------------------------|-------------------|----------------|------------------|--------------|-----------------|--------------|-----------------|
| | | Male (n=19) | Female (n=16) | <30 (n=7) | 30-50 (n=23) | >50 (n=5) | |
| Interlobular septal thickening | | 100 | 100 | 100 | 100 | 100 | 100 |
| Ground glass opacities | | 95 | 100 | 86 | 100 | 100 | 91.7 |
| Crazy-paving | | 68 | 100% | 86 | 87 | 60 | 83% |
| Sparing | Costophrenic | 57 | 50 | 78 | 48 | 80 | 80 |
| | Apices | 74 | 43 | 43 | 60 | 80 | 60 |
| | Subpleural | 63 | 50 | 78 | 52 | 80 | 57 |
| Consolidation | | 58 | 69 | 71 | 70 | 20 | 63 |
| Nodules | | 42 | 19 | 71 | 17 | 40 | 31 |
| Mass like consolidation | | 5.3 | 31 | 43 | 13 | 0 | 17 |
| Lymphadenopathy | Mediastinal | 26.3 | 6.3 | 14.3 | 21.7 | 0.0 | 17 |
| | Mediastinal/hilar | 10.5 | 0.0 | 0.0 | 0.0 | 40 | 6 |
| Pleural effusion | Unilateral | 5.3 | 0.0 | 0.0 | 4.3 | 0.0 | 2.9 |
| | Bilateral | 10.5 | 0.0 | 0.0 | 0.0 | 40 | 5.7 |
| Honeycombing | | 10.5 | 0.0 | 0.0 | 8.7 | 0.0 | 5.7 |

Table 1: Frequency (%) of HRCT findings in patients with idiopathic pulmonary alveolar proteinosis

Conclusion

This study demonstrated that the predominant HRCT presentation of idiopathic PAP was interlobular septal thickening and ground glass opacities, resulting in crazy-paving pattern. However, crazy-paving pattern may be absent in some patients with PAP and in our study ILST and GGOs without crazy-paving were seen in 17% and 14.7% of patients, respectively. In this situation high clinical suspicion in the presence of diffuse bilateral GGOs with or without septal thickening in the absence of other conditions (such as viral pneumonia, pneumocystis jiroveci pneumonia, etc.) should raise the likelihood of PAP.

This study demonstrates that the vast majority (86%) of PAP patients have costophrenic angle, apices, or subpleural sparing. Consolidation was other common CT finding of our patients. PAP is an alveolar space occupying process and therefore may present as pulmonary consolidation or mass-like consolidation. Other nonspecific findings including pulmonary nodules, mediastinal and/or hilar lymphadenopathy, mass like consolidation, pleural effusion and honeycombing were not frequently seen. These results are identical to previous studies [1,2,13,17,18,19].

In this study we found that the prevalence of crazy-paving in females was significantly higher than male patients. The cause of this difference is unknown and has not been yet reported in the previous studies.

Finally it should be mentioned that this study was done only on idiopathic PAP. Further studies are needed for comparison of imaging features of idiopathic and secondary PAP.

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